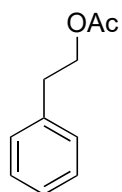
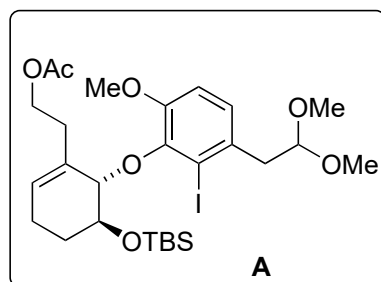


Chemoenzymatic Total Synthesis of *ent*-Oxycodone: Fourth generation

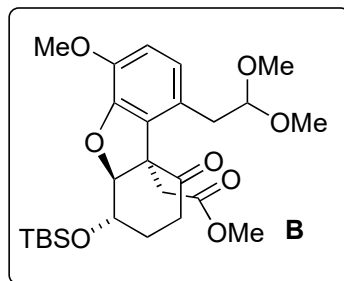
Mariia Makarova, Mary Ann A. Endoma-Arias, Helen E. Dela Paz, Razvan Simionescu, Tomas Hudlicky*
J. Am. Chem. Soc., **2019**, *10.1021/jacs.9b05033*



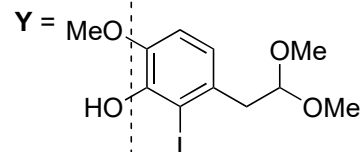
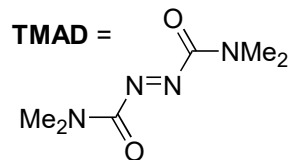
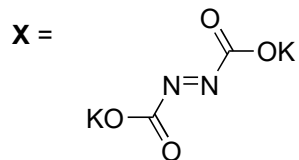
1-4



5-11



- 1) toluene dioxygenase, *E. coli* JM 109
- 2) **X**, MeOH, AcOH
- 3) TBSCl, imH
- 4) **Y**, TMAD, *n*-Bu₃P



How would you synthesize **Y**?
 Chem. Asian J. 2010, 5, 2191, see below!

- 5) Pd(OAc)₂, dppp, Ag₂CO₃
- 6) OsO₄, NMO
- 7) MsCl, NEt₃
- 8) DBU, Δ
- 9) NaOH, MeOH
- 10) TPAP, NMO, H₂O
- 11) EDCI • HCl, DMAP, MeOH

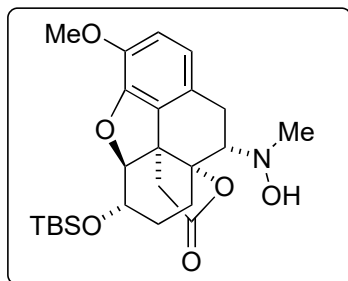
Heck
 Upjohn

Step 5: It's a name reaction! Which one?
 Step 6: It's a name reaction! Which one?

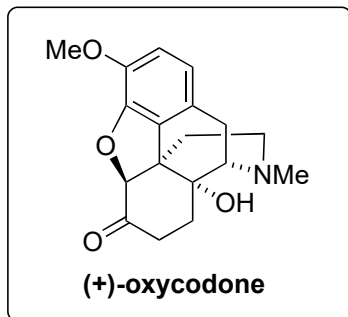
Ley-Griffith

Step 10: It's a name reaction! Which one?

12-14

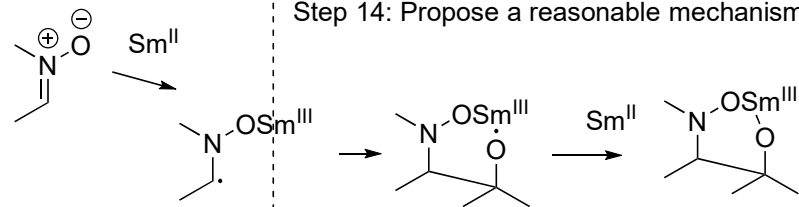


15-18



- 12) TFA, H₂O
- 13) MeNHOH • HCl, NaOAc
- 14) SmI₂

- 15) Raney-Ni, H₂
- 16) BH₃
- 17) TBAF
- 18) DMP



Step 14: Propose a reasonable mechanism!

Angew. Chem., Int. Ed. 2002, 41, 1772-1775.

